REMARKS

I. Support for the Amendments

Claims 7, 8, 11, 16, 19, 21, and 35 have been amended. In order to further prosecution in a timely manner, claims 29-32 have been cancelled without prejudice to their pursuit in an appropriate continuation or divisional application.

Support for amended claims 7, 8, 11, 16, 19, 21, and 35 can be found in the original specification and claims. Additional support for amended claims 7, 8, 11, 16, 19, 21, and 35 can be found, e.g., on pages 5-9; on page 6, lines 3-12; on page 16, lines 1-7; from page 16, line 18, to page 20, line 20; on page 17, lines 21-27; on page 18, lines 21-26; and in the Examples.

II. Status of the Claims

Claims 1-34 were originally in the application, with claims 1, 5-8, 11, 16, 19, 21, 28, 33, and 34 being the independent claims. Claims 1-4 and 6-32 were elected with traverse in Response to the Election/Restriction Requirement, with claims 1, 7, 8, 11, 16, 19, 21, and 28 being the independent claims.

In the Office Action mailed 26 December 2002, the Examiner rejected claims 1-4 and 6-32, which were all the remaining claims. In the previous Amendment, filed June 20, 2003, claims 1, 6, and 28 were cancelled, and non-elected claims 5, 33, and 34 were withdrawn without prejudice to the pursuit of such claims in a suitable continuing application.

Claims 2-4, 7-27, 29-32, and 35-43 were pending in the application, with claims 7, 8, 11, 16, 19, 21, 30, and 35 being the independent claims. In the Office Action mailed October 20, 2003, the Examiner rejected claims 2-4, 7-27, 29-32, and 35-43, all the remaining claims. In the present Office Action, mailed February 12, 2004, the Examiner has also rejected claims 2-4, 7-27, 29-32, and 35-43.

Claims 2-4, 7-27, and 35-43 are presently in the application. Claims 7, 8, 11, 16, 19, 21, and 35 are the independent claims. Claims 2-4 and 9-10 are now dependent on claim 7. Claims 12-15 are dependent on claim 11. Claims 17 and 18 are dependent on claim 16. Claim 20 is dependent on claim 19. Claims 22-27 are dependent on claim 21. Claims 36-43 are dependent on claim 35 or on claims dependent on claim 35. Claims 29-32 have been cancelled without prejudice.

III. Rejection of Claims 29-32 Under 35 U.S.C. § 112, Second Paragraph is Rendered Moot

The Examiner has rejected claims 29-32 under 35 U.S.C. §112, second paragraph (pp. 2-3; par. 5 (and 5A1)). The Examiner alleges:

> Claims 29-32 are indefinite because the method of Claim 30 is directed to a method of isolating and analyzing genetic material. The final process step in the method is directed to detecting contamination of the sample. The method also recites analyzing the sample immediately prior to this step. Thus, it is unclear whether the method is a method for detecting contamination or a method of isolating/analyzing genetic material. Since the claim contains a separate step for analyzing the sample, it appears as though the final process step may not be required to complete the claimed method. (Pp. 2-3; par. 5 (subpar. 5A1).)

In order to further prosecution in a timely manner, claims 29-32 have been cancelled without prejudice to their pursuit in an appropriate continuation or divisional application.

Applicants respectfully submit that the cancellation of claims 29-32 without prejudice renders moot the Examiner's rejection of these claims under 35 U.S.C. §112, second paragraph.

IV. Rejection of Claims 2-4, 7-27, and 30-32 Under 35 U.S.C. § 102(e) is Traversed

The Examiner has rejected claims 2-4, 7-27, and 30-32 under 35 U.S.C. §102(e) as being anticipated by Staub et al. (U.S. Patent 6,187,540; February 13, 2001) "as evidenced byo Gibco BRL Products Catalog (FTA Card, page 2-7, 1999) and Burgoyne (US Pat. 5,496,562, March 1996)." Applicants respectfully disagree.

The Examiner alleges:

> Staub et al. (herein referred to as Staub) teaches a method of newborn identification and tracking. Staub teaches a method of collecting newborn and maternal samples prior to discharge from the hospital to be collected on a single card. The card is then either stored or analyzed. Specifically, Staub teaches that a preferred sample type is **a buccal swab** which is painless to collect (col. 7, lines 5-10). Staub teaches obtaining a patient with **saliva** which produces a suspension comprising cells comprising genetic material. The saliva is applied to the buccal swab (col. 7, lines 15-16). The cells collected on the buccal cotton or sponge swabs are contacted or blotted onto FTA paper (a second solid medium). FTA paper is matrix which contains preserving means including a weak base, a chelating agent and an anionic surfactant. The sample is then forwarded to a genotyping location to obtain analysis of the genetic material (see issued Claim 1, for example)(limitations of Claim 7, 2, 4, 10). Staub teaches that it is important that the sample cards are rendered tamper-proof to ensure that samples have not been compromised (col. 4, lines 65-68). Staub teaches that the tamper-proof collection device is examined to ensure that tampering, a form of contamination, has not occurred (see Claim Id, for example)(limitations of Claim 25). **Additionally, Staub's system is directed to detect whether newborn/mother**

pairings are correct or whether there is an improper pairing such that contamination from an inappropriate sample occurred, i.e. the baby does not belong to the mother (limitations of Claim 30-32).

With respect to Claim 8, the baby or the mother, a biological sample, is obtained (limitations of Claim 9). The buccal swab isolates cells from the sample on a first solid medium. The swab is then blotted on the FTA paper.

With respect to Claim 11-15, 21-24, 26-27, a saliva sample is obtained and cells are isolated on a first solid medium. The buccal swab is then blotted on FTA paper which lyses cells for analysis of the genetic material.

With respect to Claims 16-18, the baby or the method is obtained and cells are isolated on a solid medium, the buccal swab and blotted on FTA paper. It is noted that genetic material from a virus may be present on a buccal sample.

With respect to Claims 19-20, saliva, a non-solid biological sample from a human is obtained by isolating cells from the human onto a buccal swab. The swab is then contacted with FTA paper and analyzed. (Pp. 3-5, par. 6; emphasis added.)

Applicants respectfully disagree with the Examiner's comments and traverse the anticipation rejection.

A. Claims 2-4, 7-10, 16-18, and 21-27

It should be noted that the language of claims 7 and 8 presently reads as follows:

7 (currently amended). A method of genetic analysis, wherein the method comprises:
a. **upstream processing** of a biological sample **to produce a suspension** comprising cells comprising genetic material;
b. applying the suspension to a first solid medium;
c. contacting the cells on the first solid medium with a second solid medium, wherein the second solid medium comprises a dry solid medium comprising:
    i. a matrix; and
    ii. a composition sorbed to the matrix, the composition comprising preserving means for protecting genetic material from degradation;
d. sorbing the genetic material to the second solid medium; and
e. analyzing the genetic material. (Emphasis added.)

8 (currently amended). A method of analyzing genetic material, wherein the method comprises:
a. obtaining a biological sample;
b. **processing the biological sample** to obtain one or more cells or virions comprising genetic material, **wherein the processing step comprises**:
i. **dissociating cells in the biological sample to produce a suspension**; and
ii. isolating a cell or virion on a first solid medium;
c. applying the cell or virion isolated on the first solid medium to a second solid medium, wherein the second solid medium comprises a matrix having a composition sorbed thereto, wherein the composition comprises:
i. a weak base;
ii. a chelating agent; and
iii. an anionic surfactant or detergent;
d. lysing the cell or virion and retaining the genetic material with the second solid medium;
e. analyzing the genetic material. (Emphasis added.)

Claim 16 has language ("dissociating the cells to produce a suspension comprising the cells and one or more non-cellular components") similar to claims 7 and 8. Claim 21 also has language ("processing the sample to produce a suspension comprising cells or virions comprising genetic material") similar to claims 7 and 8.

Applicants respectfully submit that a rejection under §102(e) requires the reference to contain each and every element of the rejected claim.

Applicants respectfully submit that the Examiner's use of the term "suspension" is over-broad. Collection of buccal cells or saliva is not "processing of a...sample," for example, "to produce a suspension."

A chemical suspension may be defined as follows:

suspension. A system in which very small particles (solid, semisolid, or liquid) are more or less uniformly dispersed in a liquid or gaseous medium. Hawley,

The Condensed Chemical Dictionary (10th ed.), van Nostrand Reinhold Co. (New York: 1981).

A copy of this citation is enclosed for the Examiner's convenience.

For example, a suspension may be an entity comprising a solid (e.g., cells, soil) in a liquid matrix (e.g., water). During a buccal collection, at no point does the solid (cheek cells) go into suspension. Rather, the cells directly contact the absorbent portion of the swab. Additionally, saliva, cord blood, and amniotic fluid are "natural suspensions" and, therefore, cannot be construed as having gone through "processing" (or "upstream processing") in order "to produce a suspension."

Claims 2-4 and 9-10 are dependent on claim 7, and claims 22-27 are dependent on claim 21, and the same arguments apply to these claims as well.

Therefore, neither the buccal cells nor the saliva on the swab, as described in Staub, would anticipate the presently claimed invention as described in claims 2-4, 7-10, and 21-27.

B. Claims 11-27

It should be noted that the language of claims 11 and 16 presently reads as follows:

11 (currently amended). A method of detecting and analyzing genetic material from a biological sample, wherein the method comprises:
a. obtaining a biological sample comprising a cellular component having one or more cells comprising genetic material;
b. **isolating the cellular component, on a first solid medium, from non-cellular components** in the sample;
c. **removing non-cellular components;**

d. contacting the cellular component with a second solid medium, wherein the second solid medium comprises matrix having a composition sorbed thereto, wherein the composition comprises:
    i. a weak base;
    ii. a chelating agent; and
    iii. an anionic surfactant or detergent;
e. lysing the one or more cells in the cellular component and retaining the genetic material with the second solid medium; and
f. analyzing the genetic material. (Emphasis added.)

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16 (currently amended). A method of detecting and analyzing genetic material from a biological sample from a mammal, wherein the method comprises:
a. obtaining a biological sample comprising an organ or a tissue comprising cells comprising genetic material;
b. dissociating the cells to produce a suspension comprising **the cells and one or more non-cellular components**;
c. **isolating the cells on a first solid medium**;
d. **removing substantially all the non-cellular components**;
e. contacting the cells on the first solid medium with a second solid medium, wherein the second solid medium comprises a matrix having a composition sorbed thereto, wherein the composition comprises:
    i. a weak base;
    ii. a chelating agent; and
    iii. an anionic surfactant or detergent;
f. lysing the cells and retaining the genetic material with the second solid medium; and
g. analyzing the genetic material. (Emphasis added.)

Similar language is found in claim 19 ("isolating the component of interest on a first solid medium and removing substantially all of the remaining components of the sample") and in claim 21 ("isolating the cells or virions on a first solid medium and removing substantially all of the remaining components of the sample").

Applicants respectfully submit that a rejection under §102(e) requires the reference to contain each and every element of the rejected claim.

Staub does not describe removal of non-cellular or other remaining components of the sample. Staub simply describes a buccal or saliva sample being taken on a swab, for example, and then transferred to a card or similar device. In claims 11, 16, 19, and 21, the desired component (e.g., a cell) is isolated on the first solid medium and "remaining components" or "non-cellular components" are removed. Staub does not provide a method for isolating a component of interest, such as a cellular component and removing other components.

Claims 12-15 are dependent on claim 11, claims 17-18 are dependent are claim 16, claim 20 is dependent on claim 19, and claims 22-27 are dependent on claim 21, and the same arguments apply to these claims as well.

Therefore, neither the buccal cells nor the saliva on the swab, as described in Staub, would anticipate the presently claimed invention as described in claims 11-27.

C. Claims 30-32

In order to further prosecution in a timely manner, claims 29-32 have been cancelled without prejudice to their pursuit in an appropriate continuation or divisional application. The Examiner's rejection of claims 30-32 is rendered moot.

V. Rejection of Claims 4 and 7 Under 35 U.S.C. §102(e) is Traversed

The Examiner has rejected claims 4 and 7 under 35 U.S.C. §102(e) as being anticipated byo Kathariou et al. (U.S. Patent 6,503,747; January 7, 2003) "as evidenced by

www-biology.ucsd.edu/labs/aroian/protocols/electroblot.htm (pp. 5-6, par. 7). Applicants respectfully disagree.

The Examiner alleges:

> Kathariou et al. (herein referred to as Kathariou) teaches a method for analyzing genetic material. Mutants from 96-well plates were inoculated with a 48 prong replicating device on agar plates (first solid medium) and grown overnight. Bacterial colonies were transferred onto nitrocellulose membranes (second solid mediums) **presoaked in Twobin transfer buffer**. The nitrocellulose membranes were **dried and processed** using immunoblot procedures (col. 18, lines 30-40)(limitations of Claim 7). The colonies were dissociated **from the culture plates** (limitations of Claim 4).
>
> The art teaches Towbin transfer buffer is a solution of Tris, Glycine, SDS, MeOH at a pH of about 8.3. Towbin is considered a preserving means.... (Pp. 5-6; par. 7; emphasis added.)

Applicants respectfully disagree with the Examiners comments and traverse the anticipation rejection.

It should be noted that claim 7 presently reads as follows:

> 7 (currently amended). A method of genetic analysis, wherein the method comprises:
> a. upstream processing of a biological sample to produce a suspension comprising cells comprising genetic material;
> b. applying the suspension to a first solid medium;
> c. contacting the cells on the first solid medium with a second solid medium, **wherein the second solid medium comprises a <u>dry</u> solid medium** comprising:
> i. a matrix; and
> ii. a composition sorbed to the matrix, the composition comprising preserving means for protecting genetic material from degradation;
> d. sorbing the genetic material to the second solid medium; and
> e. analyzing the genetic material. (All emphasis added.)

Applicants respectfully submit that a rejection under §102(e) requires the reference to contain each and every element of the rejected claim. Claim 7 has already been analyzed with respect to Staub, and some of those arguments also apply to Kathariou.

According to Kathariou,

> Isolated transconjugants were inoculated into individual wells of 96-well culture plates containing 200 µl of brain heart infusion broth with streptomycin and either tetracycline or erythromycin. The 96-well plates were frozen at -70°C. The mutants from the 96-well plates stored at -70°C were inoculated with a 48-prong replicating device on Tryptic Soy Broth – 0.7% Yeast Extract – 1.2% Agar Plates with appropriate antibiotics and grown overnight at 22°C. Bacterial colonies were transferred onto nitrocellulose membranes (Micron Separations Inc.) **presoaked** in Towbin **transfer buffer** [citation omitted]. **The nitrocellulose membranes were air dried for 15 min.** and processed according to standard immunoblot procedures.... (Col. 17, l. 8, to col. 18, l. 36; emphasis added.)

Clearly, the membranes of Kathariou were wet with transfer buffer at the time of transfer and needed to be dried prior to processing. According to the present language of claim 7, however, "the second solid medium comprises a **dry** solid medium," rather than the wet medium of Kathariou.

The present language of claim 4 reads as follows:

> 4 (previously presented). The method of claim 7, wherein the **upstream processing step** further includes **dissociating the cells** of the biological sample. (Emphasis added.)

Because claim 4 is dependent on claim 7, the arguments regarding claim 7 also apply here. In addition, the Examiner alleges that Kathariou anticipates claim 4, because the colonies were dissociated from the "culture plates." It is unclear whether the "culture plates" the Examiner mentions refer to the 96-well plates or to the agar plates. If the former,

then there is **no evidence** in Kathariou that the cells were adhering to the 96-well plate and **no discussion of upstream processing** including dissociating the cells **to produce a suspension** prior to the application of the cells to the first solid medium; if the latter, the dissociation of the cells from the **agar** plate, to which the Examiner refers as the first **"solid"** medium, has no bearing on claim 4, which is directed to dissociation of cells to produce a **suspension** during the **upstream processing** step **prior to the application of the suspension to the first solid medium**. Applicants respectfully point out that the dissociation of the cells in claim 4 refers to the upstream processing step.

Accordingly, Kathariou fails to anticipate claims 4 and 7 of the present application.

Applicants respectfully submit that the present claims 4 and 7 fulfill the requirements of 35 U.S.C. §102(e) and request the Examiner's reconsideration of these claims accordingly.

VI. Rejection of Claims 35-43 Under 35 U.S.C. § 103(a) Is Traversed

The Examiner has rejected claims 35-43 under 35 U.S.C. 103(a) as being unpatentable over Staub et al. (U.S. Patent 6,187,540; February 13, 2001) "as evidenced by Gibco BRL Products Catalog (FTA Card, page 2-7, 1999) and Burgoyne (U.S. Pat. 5,496,562, March 1996) in view of Robertson (U.S. Pat. 6,153,104, November 2000)." Applicants respectfully disagree.

After outlining the arguments made for anticipation of claims 2-4, 7-27, and 30-32 (already quoted *supra*), the Examiner alleges, in pertinent part:

The instant specification teaches FTA coating spontaneously lyses leukocytes releasing the genomic DNA (page 15 ,lines 5-6). The instant specification cites the chemical coating solution as described in 5,496,562....

Staub does not specifically teach obtaining the first matrix using a vacuum.

However, Robertson teaches a method of body fluid separation. The method uses a device comprising a chamber, a cooperating filter, a second chamber, where the first and second chamber has a connection to vacuum with filters on each side and a removable closure in the form of end caps. As seen in Figure 1 the device is provided. Robertson teaches that the invention provides equipment of notable simplicity and relatively low cost with method steps well within the capabilities of junior members of laboratory staff, to enable separation of a body fluid into various of its component (col. 1, lines 30-35). Robertson teaches obtaining a biological sample, such as saliva (col. 3, lines 25-26). The biological sample is in a suspension comprising genetic material, as saliva comprises cells. **An apparatus comprising a chamber, two solid mediums, a vacuum means is seen in Figure 1.** The sample is applied to one side of a filter, vacuum is applied to the opposite side of the filter to draw the liquid, leaving the cells on the first solid support. Robertson teaches that to gather the cell contents of the leukocyte cells, it is most desirable that a filter membrane is provided to isolate the DNA content of the cells form other cell debris washed from the filter (col. 4, lines 60-65).

Therefore, it would have been prima facie obvious to one of ordinary skill at the time the invention was made to have modified the method of Staub to include the vacuum steps of Robertson to prepare the first solid support. The ordinary artisan would have been motivated to have taken a saliva sample and place the sample in a vacuum to obtain a solid support comprising cells. Given the teachings of Staub, the ordinary artisan would have taken the solid support comprising the cells and blotted them onto FTA paper for the express benefit of preserving the genetic material in an inexpensive and space conserving manner (col. 7, lines 30-35 of Staub). Robertson teaches that using a vacuum allows for low cost procedures using relatively simple equipment with attendant procedures well within the capabilities of junior members of laboratory staff, to enable separation of a body fluid into various components (col. 1, liens 30-35 of Robertson). The ordinary artisan would have recognized the simplicity of separation of cells using the vacuum and would have been motivated to have separated cells using the method described by Roberston. Once the cells were immobilized on a solid support using the method of Robertson, the ordinary artisan would have been motivated to have transferred the cells to FTA paper. Staub teaches that cells may be transferred from solid supports by blotting onto FTA paper. FTA paper is a convenient method for storing blood samples for DNA testing. Therefore, the ordinary artisan would have been motivated to have collected any number of samples using the vacuum method of Staub to immobilize cells prior to blotting them onto FTA paper for the benefit of storage and preservation of the sample for later analysis. (Pp. 8-10, par. 9; emphasis added.)

Applicants respectfully disagree with the Examiner's comments and traverse the obviousness rejection.

The present language of claim 35 reads as follows:

35 (currently amended). A method of detecting and analyzing genetic material from a biological sample, wherein the method comprises:

a. obtaining a biological sample;

b. **processing the biological sample to produce a suspension** of one or more cells or virions comprising genetic material and one or more non-cellular or non-viral components;

c. providing an apparatus comprising:

i. **a chamber** for containing a fluid including a suspension of cells or virions therein, the chamber comprising:

- an opening therethrough; and
- **a first solid medium** removably disposed over the opening;

ii. vacuum means for drawing the fluid from the chamber and through the first solid medium and depositing the cells or virions on the first solid medium;

iii. **a second solid medium** wherein **the second solid medium comprises a dry solid medium** comprising:

- a matrix; and
- a composition sorbed to the matrix, the composition comprising preserving means for protecting the genetic material from degradation;

d. placing a fluid comprising the suspension in the chamber;

e. using the vacuum means to draw the fluid from the chamber and through the first solid medium and to deposit the cells or virions on the first solid medium and to remove substantially all of the non-cellular and non-viral components;

f. contacting the cells or virions on the first solid medium with the second solid medium;

g. releasing the genetic material from the cells or virions and retaining the genetic material with the second solid medium; and

h. analyzing the genetic material. (Emphasis added.)

Staub has already been discussed at length, *supra*, and the same arguments also apply here. For example, the Examiner's argument concerning saliva, as opposed to the "processing" of "the biological sample to produce a suspension of one or more cells or

virions" has previously been discussed, and the same arguments, as well as the other arguments made *supra*, apply here.

Moreover, there is no disclosure or suggestion in Staub of a chambered device with one or more solid media and a vacuum. Staub neither discloses nor suggests the device described by Robertson, and Staub likewise neither discloses nor suggests the claimed invention of claims 35-43.

While Robertson (see, e.g., cols. 4-5) describes the use of "water, isotonic saline, an appropriate chemical lysing agent or a compatible cell detergent" to lyse **leukocytes after they have been already entrapped** within the filter, **it does not describe or suggest a "composition sorbed to the matrix"** to produce a "**dry** solid medium" to which a **sample is subsequently exposed.** (In at least **one embodiment**, Robertson **does not lyse the cells at all** (col. 2, ll. 63-65).)

Moreover, the method and apparatus of **Robertson require the use of at least two chambers** to hold the liquids used, **separated by a single filter** (claims), rather than the **single chamber** with **two solid media** provided by claim 35. Nowhere in Robertson is there even a suggestion of the single chamber with two solid media provided by claim 35, much less transfer of the cells or virions **directly** from the first solid medium to the second solid medium.

In fact, **the material shown in Figure 1** at the bottom of the second chamber (in cap **6**), to which an arrow has been drawn with the word "filter" inscribed, is **not the second medium** of the present invention, **but is described as "waste material"** (col. 4, ll. 44-45) comprising "plasma and red cell content of the blood" (col. 4, ll. 38-39), **which is not part of the device**, but which is discarded with the cap **6** (col. 4, ll. 44-45).

Finally, the Examiner's argument that the invention of Robertson "provides equipment of notable simplicity and relatively low cost with method steps will within the capabilities of junior members of laboratory staff" is irrelevant to the claim language.

Likewise, there is **no suggestion in either** of the references **to combine the teachings of Robertson with Staub**. As noted *supra*, Robertson simply discloses a method of isolating cells using a filter and then optionally lysing them using liquid chemical treatments. There is no suggestion of a solid medium comprising a matrix with a **composition already sorbed to the matrix prior to contact with cells** in a sample. In contrast, **Staub focuses on the application of whole cells onto a treated solid medium** (FTA paper) **capable of lysing the cells directly without the need for a liquid lysate**. As a result, **Staub teaches away from Robertson**, because one of ordinary skill in the art reading Robertson would assume that, because the method of Robertson requires isolation of the cells on the filter prior to lysis with a liquid chemical treatment, it would not be applicable for the treated solid medium of Staub, resulting in **a doubling of the lysis steps**. Nowhere is there any discussion in Robertson of **transferring the cells from the first solid medium to a second solid medium prior to lysis**.

Claims 36-43 are dependent, either directly or indirectly, on claim 35, and the arguments with respect to claim 35 likewise apply to claims 36-43.

Applicants respectfully submit that the present claims 35-43 fulfill the requirements of 35 U.S.C. §103(a) and request the Examiner's reconsideration of these claims accordingly.

VII. Conclusion

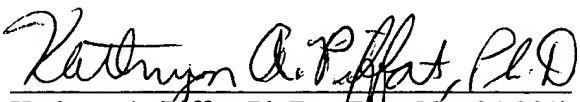
It is believed that all outstanding rejections have been addressed by this submission and that all the claims are in condition for allowance. If discussion of any amendment or remark made herein would advance this important case to allowance, the Examiner is invited to call the undersigned as soon as convenient.

In view of the foregoing amendments and remarks, the present application is respectfully considered in condition for allowance. An early reconsideration and notice of allowance are earnestly solicited.

Applicants believe that no extension of time is required. If, however, a petition for an additional extension of time is required, then the Examiner is requested to treat this as a conditional petition for an additional extension of time. Although it is not believed that any fee is required, in addition to the fee submitted herewith, to consider this submission, the Commissioner is hereby authorized to charge our deposit account no. 04-1105 should any fee be deemed necessary.

Respectfully submitted,

Date: May 11, 2004



Kathryn A. Piffat, Ph.D., (Reg. No. 34,901)
Intellectual Property Practice Group
EDWARDS & ANGELL, LLP
P.O. Box 55874
Boston, Massachusetts 02205
Telephone: 617-439-4444